REMARKS

Claims 1-64 were pending in the application. Claims 2, 43-45, and 49-64 have been cancelled without prejudice or disclaimer. Claims 1, 3-12, 17, 18, 19, 20-28, 29, 32, and 34 have been amended. Accordingly, claims 1, 3-42 and 46-48 will be remain pending in the application upon entry of the amendments presented herein.

Support for the amendment of the claims can be found throughout the specification and claims as originally filed. In particular, support for the amendment of claim 1can be found in the specification at least, for example, on page 7, line 29, and in claims, 1, 2 and 11 as originally filed; support for the amendment of claims 19 and 20 can be found in claims 19 and 20, respectively, as originally filed; and support for the amendment of claim 34 can be found in the specification at least, for example, on page 8, lines 27-28.

Claims 3-12, 17, 18, 29 and 32 were amended to remove dependency from cancelled claim 2, and therefore, support for the amendment to claims 3-12, 29 and 32 may be found at least, for example, in claims 3-12, 29 and 32 as originally filed. Claims 20-28 were amended to standard compound claim format, and therefore, support for the amendment to claims 20-28 may be found at least, for example, in claims 20-28 as originally filed. No new matter has been added.

Attached hereto as Appendix A is a marked-up version of the changes made to the specification and the claims by the current amendments. Appendix A is captioned **"Version with Markings to Show Changes Made."** Also attached hereto as Appendix B is a complete set of the claims that will be pending upon entry of the amendments presented herein.

Amendment and cancellation of the claims is not to be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action or previous Office Actions, and was done solely to expedite prosecution of the instant application. Applicant hereby reserves the right to prosecute the claims as originally filed, or similar claims, in one or more continuation applications and/or divisional applications.

Election/Restriction

Claims 43-45 and 49-64 have been withdrawn from consideration as directed to non-elected subject matter. Accordingly, claims 43-45 and 49-64 have been cancelled without prejudice or disclaimer. Applicant hereby reserves the right to prosecution the non-elected subject matter of the cancelled claims in one or more divisional patent applications.

Claim Rejections - 35 U.S.C. §112

Rejection of Claims 1, 14-16, 19-40, and 46-48 under 35 U.S.C. §112, Second Paragraph

Claims 1, 14-16, 19-40, and 46-48 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Office Action indicates that the term "tail group" is not reasonably defined within the scope of the invention. Applicant disagrees and respectfully traverses this rejection.

However, without acquiescing in any way to the rejection and in order to expedite prosecution, Applicant has amended claim 1 to recite the tail group of formula IA specifically recited in claim 2 as originally filed. Therefore, Applicant submits that this rejection no longer applies to claim 1 as amended.

In addition, the Office Action indicates that the term "comprising" in claims 19 and 20 is indefinite, and that claims 20-28 are unclear as written, and the Examiner suggests amending the claims in accordance with proper format. Applicant respectfully traverses the rejection.

However, without acquiescing in any way to the rejection and in order to expedite prosecution, Applicant has amended claims 19-28 by deleting the term comprising in claims 19 and 20 and otherwise redrafting claims 20-28 as standard compound claims. Therefore, Applicant submits that these rejections no longer apply to claims 19-28 as amended.

In addition, the Office Action sets forth the allegation that claims 29 and 32 are unclear because the meaning of the term 'modulates' includes both enhancement and inhibition. Applicant respectfully traverses this rejection.

Applicant invites the Examiner's attention to the definition of the term "modulator" in the specification at page 17, lines 23-37. Upon a reading of this definition, one of ordinary skill in the art will readily appreciate that the term is intended to include both induction and/or potentiation (*i.e.*, enhancement) as well as inhibition and/or down regulation. Thus, when claims 29 and 32 are read in light of this excerpt of the specification, it is clear that claims 29 and 32 are compound claims that are directed to the modulator embodiment of the invention. Specifically, claim 29 is directed to compounds that modulate (*i.e.*, induce and/or inhibit) the autoinducer activity of 2-heptyly-3-hydroxy-4-quinolone, with claims 30 and 31, depending therefrom, specifying the type of modulation (inhibition and synergistic enhancement, respectively). Therefore, Applicant submits that claims 29 and 32 meet the requirements of definiteness and clarity imposed by the second paragraph of Section 112.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection of the claims 1, 14-16, 19-40, and 46-48 under the second paragraph of 35 U.S.C. §112.

Duplicate Claims

The Office Action indicates that should claim 1, 2 or 19 be found allowable, claims 20-27 will be objected to as duplicative; and should claims 1 or 2 be found allowable, claims 29-32, and 32 will be objected to as duplicative. The Office Action further indicates that claims 20-27 do not further limit the compound of claim 1, 2, or 19, nor do claims 29-30, 32 further limit the compound of claims 1 or 2. Applicant respectfully disagrees, and will address this matter further upon a finding that claims 1 and 19 are allowable.

The Office Action also indicates that claim 33 is duplicative of claim 34, and is objected to under 37 CFR 1.75. Applicant has amended claim 34 to correct a typographical error, thereby obviating the objection.

Claim Rejections - 35 U.S.C. §102

Rejection of Claims 1, 2, 4, 10-14, 19-28 32-42, 46-48 under 35 U.S.C. §102(a)

Claims 1, 2, 4, 10-14, 19-28 32-42, 46-48 were rejected under 35 U.S.C. §102(a) as anticipated by Pesci *et al.* PNAS, 1999, 96(20):11229 (the Pesci *et al.* reference). Applicant respectfully traverses the rejection.

The Pesci *et al.* reference names as authors the same six individuals who are named as co-inventors on the instant application, as well as Susan McKnight. In this context of co-authorship, M.P.E.P. §715.01(c) provides in pertinent part as follows:

> "Where the applicant is one of the co-authors of a publication cited against his or her application [under 35 U.S.C. §102(a)], he or she may overcome the rejection.....by filing a specific affidavit or declaration under 37 C.F.R. §1.132 establishing that the article is describing applicant's own work. An affidavit or declaration by applicant alone indicating that applicant is the sole inventor and that the others were merely working under his or her direction is sufficient to remove the publication as a reference under 35 U.S.C. §102(a). *In re Katz*, 687 F.2d 450, 215 U.S.P.Q. 14 (CCPA 1982)."

Applicant asserts that co-author Susan McKnight is not a co-inventor of the subject matter disclosed and claimed in the instant application, and was merely a technician working under the direction and supervision of Everett P. Pesci, co-inventor and lead author of the Pesci et *al.* paper. In support of this assertion, Applicant submits herewith, pursuant to 37 C.F.R. §1.132, the Declaration of Everett P. Pesci who declares that: the Pesci *et al.* paper discloses his own research and that of the above-identified co-inventors; co-author Susan McKnight is not an inventor of subject matter disclosed and claimed in the above-referenced patent application; and Susan McKnight worked under his direction and supervision during the research that was reported in the Pesci *et al.* paper.

Applicant submits that the Declaration of co-inventor Everett P. Pesci effectively removes the Pesci *et al.* paper as a reference under 35 U.S.C. §102(a), and therefore, respectfully request reconsideration and withdrawal of the rejection of claims 1, 2, 4, 10-14, 19-28 32-42, 46-48 under 35 U.S.C. §102(a)/ over the Pesci *et al.* paper.

Rejection of Claims 1, 14, 15, and 20-40 under 35 U.S.C. §102(b)

Claims 1, 14, 15, and 20-40 were rejected under 35 U.S.C. §102(b) as anticipated by Dekker *et al.*, U.S. Patent No. 5,942,619 (or WO 97/12868). The Office Action asserts that Dekker recites compounds that are encompassed by the instant claims.

Applicant has amended claim 1 such that R_5 is not H. Support for the amendment to claim 1 may be found in the specification at least, for example, on page 7, line 29 and in claim 11 as originally filed. Applicant submits that the claims as amended no longer encompass the compounds of Dekker, as such compounds require that R_5 is H. Therefore, Applicant respectfully requests withdrawal of the rejections of claims 1, 14, 15, and 20-40 under 35 U.S.C. §102(b) and favorable reconsideration.

Rejection of Claims 1-4, 9, 12, 14 and 20-40 under 35 U.S.C. §102(b)

Claims 1-4, 9, 12, 14 and 20-40 were rejected under 35 U.S.C. §102(b) as anticipated by Guilhon (Phytochemistry, 1994, 37(4), 1193-1195). The Office Action asserts that Guilhon recites compounds that are encompassed by the instant claims.

As noted above, Applicant has amended claim 1 such that R_5 is not H, and submit that the claims as amended no longer encompass the compounds of Guilhon, as such compounds require that R_5 is H. Therefore, Applicant respectfully requests withdrawal of the rejections of claims 1-4, 9, 12, 14 and 20-40 under 35 U.S.C. §102(b) and favorable reconsideration.

Rejection of Claims 1, 14, 15, and 20-40 under 35 U.S.C. §102(b)

Claims 1, 14, 15, and 20-40 were rejected under 35 U.S.C. §102(b) as anticipated by Lee *et al.* (J. Liq. Chrom. & Rel. Technol., 1997, 20(1), 63-78). The Office Action asserts that Lee recites compounds that are encompassed by the instant claims.

As noted above, Applicant has amended claim 1 such that R_5 is not H, and submit that the claims as amended no longer encompass the compounds of Lee, as such compounds require that R_5 is H. Therefore, Applicant respectfully requests withdrawal of the rejections of claims 1, 14, 15, and 20-40 under 35 U.S.C. §102(b) and favorable reconsideration.

Rejection of Claims 1-4, 12, 14 and 20-34 under 35 U.S.C. §102(b)

Claims 1-4, 12, 14 and 20-34 were rejected under 35 U.S.C. §102(b) as anticipated by Beifuss (Synlett, 1997, 3, 313-315). The Office Action asserts that Beifuss recites compounds that are encompassed by the instant claims.

As noted above, Applicant has amended claim 1 such that R_5 is not H, and submit that the claims as amended no longer encompass the compounds of Beifuss, as such compounds require that R_5 is H. Therefore, Applicant respectfully requests withdrawal of the rejections of claims 1-4, 12, 14 and 20-34 under 35 U.S.C. §102(b) and favorable reconsideration.

Rejection of Claims 1-4, 12, 14, 20-40, and 46 under 35 U.S.C. §102(b)

Claims 1-4, 12, 14, 20-40, and 46 were rejected under 35 U.S.C. §102(b) as anticipated by Debitus (J. Marine Biotechnology, 1998, 6, 136-141). The Office Action asserts that Debitus recites compounds that are encompassed by the instant claims.

As noted above, Applicant has amended claim 1 such that R_5 is not H, and submit that the claims as amended no longer encompass the compounds of Debitus, as such compounds require that R_5 is H. Therefore, Applicant respectfully requests withdrawal of the rejections of claims 1-4, 12, 14, 20-40, and 46 under 35 U.S.C. §102(b) and favorable reconsideration.

Claim Rejections - 35 U.S.C. §112

Rejection of Claims 1-42 and 46-48 under 35 U.S.C. §112, First Paragraph

Claims 1-42 and 46-48 have been rejected under 35 U.S.C. §112, first paragraph. The Office Action sets forth the allegation that specification is only enabling for making and using 2-heptyl-3-hydroxy-4-quinolone, and that the specification otherwise lacks an enabling disclosure to make and use the invention commensurate in scope with the claims of the instant invention. Applicant respectfully traverses the rejection.

At the outset, Applicant would like to clarify that claim 1 is drawn to compounds of formula I (quinolone derivatives). Such compounds can be autoinducers or they can be modulators of the activity of autoinducer compounds, as well as modulators of the activity of LasR and/or RhlR proteins. This distinction is seen, for example, in claim 20. Claim 20 is distinct from claims 1 and 19, in that it is directed to the subgeneric group of compounds of formula I that are autoinducer molecules. Thus, as noted in the Office Action, the compounds of the invention are useful, *e.g.*, for inhibiting the infectivity of *Pseudomonas aeruginosa* (and, therefore, are useful for treating an immunocompromised subject infected therewith), and for regulation of gene expression.

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The Office Action admits on page 7 that the level of skill in the autoinducer art is high, based on Pearson, Bycroft, Livinghouse, and Pesci. In accordance with 35 U.S.C. §112, first paragraph, it is unnecessary for Applicant to provide written description of that which is known by the skilled artisan. In fact, M.P.E.P. §2164.08 provides in pertinent part as follows (emphasis added):

> The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without `undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). **Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted**. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art.

Therefore, based on the Office Action's admission of the high level of skill in the art, Applicant submits that these references should provide supporting enabling disclosure for the autoinducer compounds in the instant invention.

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The Office Action cites the Bycroft reference in support of the allegation that not only is there a high degree of unpredictability in the autoinducer art, but that it is known that "a small change in the structure of the compound would drastically change its biological activity, as shown by the structurally similar autoinducer compounds [of Bycroft]."

Applicant respectfully traverses this rejection. Bycroft discloses autoinducer compounds and investigates the autoinducer activity of these compounds in terms of induction, *i.e.*, of luminescence. The claims of the instant invention are directed to ***compounds*** having a range of activities, *e.g.*, modulating (both enhancement and inhibition) of the activity of LasR and/or RhlR proteins and quinolone autoinducer compounds (*e.g.*, 2-heptyl-3-hydroxy-4-quinolone), as well as, though not necessarily, autoinducer activity (*e.g.*, 2-heptyl-3-hydroxy-4-quinolone). The type of activity that a compound of the invention has can be easily determined by one of ordinary skill in the art using known methods and those described in the instant specification (*e.g.*, the PQS assay described on pages 19-23 and in Example 1 on page 28) without undue experimentation.

Applicant notes that the compounds of Bycroft are ***homoserine lactones***; molecules whose core ring structure is structurally distinct from the core ring structure of the **quinolone** compounds of the instant invention. Therefore, assuming, *arguendo*, that the Bycroft reference demonstrates any relevant unpredictability, the determinations of structural changes on the activities of the compounds disclosed in Bycroft cannot be considered dispositive of the predictability/unpredictability of the changes in activity of the compounds of the instant invention upon similar structural changes. Accordingly, the position taken in the Office Action based on Bycroft is mere conjecture, at least as far as the claimed compounds are concerned.

The Office Action also makes reference to two molecules described in the instant invention on page 24 that are structurally similar to 2-heptyl-3-hydroxy-4-quinolone but did not activate the *lasB'-lacZ* strain in PAO-R1 (*lasR*$^-$)(pTS400) (see page 24, lines 24-35 of the specification). Although these two compounds did not show autoinducer activity similar to that of 2-heptyl-3-hydroxy-4-quinolone, Applicant submits that this does not mean that the

compounds are not active as modulators (*e.g.*, inhibitors of the autoinducer activity of 2-heptyl-3-hydroxy-4-quinolone). Therefore, these two compounds do not demonstrate the general unpredictability in the art that the Office Action asserts. However, without acquiescing to the rejection and in order to expedite prosecution of the application, Applicant has amended claim 1 such that the compounds noted on page 24 are not within the scope of the claim as amended. Therefore, at a minimum, Applicant submits that the claims as amended are fully enabled for the reasons set forth herein, and that this rejection no longer applies.

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The Office Action further contends that the procedures for making the compounds of formula I other than 2-heptyl-3-hydroxy-4-quinolone (especially where the compounds of the invention where the tail group is not fully described), "are not seen in the specification, but are required." Applicant traverses this rejection, and respectfully refers the Examiner to M.P.E.P. § 2164.08, quoted above, as well as to the references cited in the Office Action under 35 U.S.C. §102 (a) and (b). These references describe the synthesis of quinolone derivatives. Although these derivatives are not encompassed by the claims of this invention, the references nevertheless provide a substantial body of knowledge in the art of synthesis of quinolone derivatives. Thus, one of ordinary skill in the art would have these references available for use in the preparation of the compounds of the invention (including compounds with a variety of tail groups), eliminating the need for Applicant to specifically disclose the preparation of all of the possible compounds within the claimed genus. However, without acquiescing to the rejection and in order to expedite prosecution of the instant application, Applicant has amended claim 1 to include a specific structural recitation of the tail group. Therefore, at a minimum, Applicant submits that the claims as amended are fully enabled for the reasons set forth herein, and that this rejection no longer applies.

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The Office Action states on page 8 that

> [a]n example for a compound that 'modulates' the activity of PQS, either enhances or inhibits the autoinducer activity of PQS, 'modulates' or antagonizes

the activity of Las R and/or the RhlR proteins as recited in the instant claims 29-34 has not been described in the specification.

Applicant respectfully disagrees with this analysis and asserts that the term 'modulates,' which is defined in the specification at page 17, lines 23-37 (as discussed above), would be clear to one of ordinary skill in the art. It would be readily appreciated that the term is intended to include both induction and/or potentiation (*i.e.*, enhancement) as well as inhibition and/or down regulation of the autoinducer activity of 2-heptyly-3-hydroxy-4-quinolone, and the activity of the LasR and RhlR proteins.

In particular, the skilled artisan would understand that modulators of the autoinducer activity of 2-heptyly-3-hydroxy-4-quinolone could be determined without undue experimentation by adding the prospective modulator (a compound within the scope of claim 1) to the bioassay for the PQS as described on page 28 (Example 1), and determining the result of such addition on the activity of 2-heptyly-3-hydroxy-4-quinolone.

The LasR and RhlR proteins are the putative autoinducer transcriptional regulator proteins as described in the Background of the specification on page 2 lines 33-34. Therefore, it would be clear to one of ordinary skill in the art that modulators of the LasR and/or RhlR proteins could be determined by measuring the affect of the addition of quorum signaling molecules associated with the activity of these proteins, *i.e.*, modulators of LasR would affect the response to exogenously added N-(3-oxododecanoyl) homoserine lactone, while the modulators of RhlR would affect the response to exogenously added N-butyryl homoserine lactone. Support for this assertion is set forth in the application on page 2, lines 33-39 and pages 19-21, in the section of the specification entitled "Discovery of a Novel Cell-to-Cell Signal".

Moreover, Applicant submits that the Office Action in effect would impose an additional requirement, one not contained in 35 U.S.C. §112, of a working example or examples to enable the breadth of the claims reciting modulators of quinolone autoinducers and Las R and/or the RhlR proteins. However, Applicant asserts that a working example is not required for enablement. See, *Shanks v. Scheffer*, 204 U.S.P.Q. 781, 783 (Pat. Bd. Inter. 1979). Moreover, "there is no magical relation between the number of representative examples and the breadth of the claims". *In re Borkowski and VanVenroy*, 164 U.S.P.Q. 642, 646 (C.C.P.A. 1970). Section 112 only requires that the "specification contain a written description of the invention, and the manner and process of making and using it". Moreover, the disclosure of invention set forth by Applicant must be given the presumption of correctness and operativeness by the PTO, and the only relevant concern of the PTO under the circumstances should concern the truth of the

assertions contained in the application. *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (C.C.P.A. 1967); see also, *In re Bowen*, 492 F.2d 859, 181 U.S.P.Q. 48 (C.C.P.A. 1974).

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In view of the foregoing, Applicant submits that the claims of the application as originally filed and, at a minimum claim 1, as amended herein, is fully enabled by the specification.

Specification/Drawings

The specification has been objected to because the figures in the specification do not come within the purview of 37 CFR 1.58(a). The Office Action further states that formal drawings are required as well as a brief description of drawings.

Applicant appreciates the United States Patent and Trademark Office having published the application, with the figures embedded within the text. Upon an indication of allowable subject matter, Applicant will file a substitute specification, including a brief description of drawings, as well as formal drawings.

SUMMARY

In view of the foregoing, entry of the amendments and remarks presented herein, reconsideration and withdrawal of all the objections and rejections, and allowance of the application with all pending claims are respectfully requested. If a telephone conversation with Applicant's attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,

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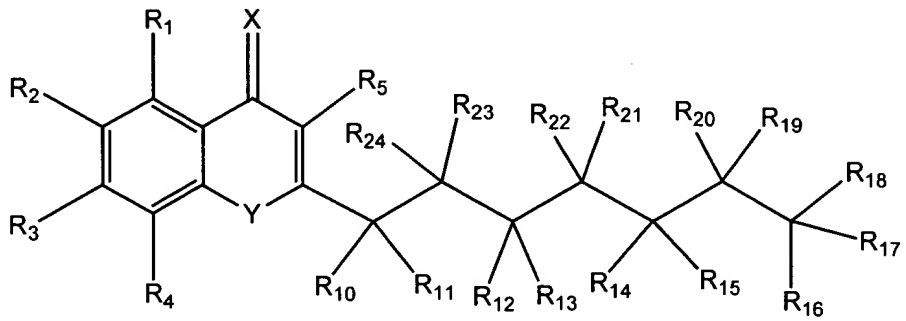
Dated: December 9, 2002

APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims

1. (Amended) A compound of formula I

(I) 

wherein:

R_1-R_4 are independently H, alkyl, alkenyl, alkynyl, OH, NH_2, SH, O-R_6, N-R_7R_8, or a halogen;

R_5 is [H,] SH, OH, O-R_6, or N-R_7R_8;

R_6 is H or C_1-C_4 alkyl;

R_7 and R_8 are independently H, C_1-C_4 alkyl, O, or S;

X [and Y are independently] is S, O, or N-R_9;

Y is N-R_9;

R_9 is H, O, S, or C_1-C_4 alkyl;

[Q is a tail group]R_{10}-R_{13} are independently H, C_1-C_4 alkyl, OH, NH_2, SH, O-R_{25}, N-$R_{26}R_{27}$, or a halogen, or R_{10} and R_{11} taken together form a carbonyl, a sulfonyl or an imino moiety, or R_{12} and R_{13} taken together form a carbonyl, a sulfonyl or an imino moiety;

R_{14}-R_{24} are independently H, C_1-C_4 alkyl, OH, NH_2, SH, O-R_{25}, N-$R_{26}R_{27}$, or a halogen;

R_{25} is H or C_1-C_4 alkyl; and

R_{26} and R_{27} are independently H, C_1-C_4 alkyl, O, or S; and

salts thereof.

3. (Amended) The compound of claim [2]1 that is different than 2-heptyl-3-hydroxy-4-quinolone.

4. (Amended) The compound of claim [2]1, wherein R_{16}, R_{17}, and R_{18} are H.

5. (Amended) The compound of claim [2]1, wherein R_2 is halogen.

6. (Amended) The compound of claim [2]1, wherein R_3 is halogen.

7. (Amended) The compound of claim [2]1, wherein R_4 is halogen.

8. (Amended) The compound of claim [2]1, wherein X is S or N-R_9.

9. (Amended) The compound of claim [2]1, wherein Y is O, S, or N-R_9 and wherein R_9 is C_1-C_4 -alkyl.

10. (Amended) The compound of claim [2]1, wherein R_5 is H, SH, O-R_6, or N-R_7R_8, and wherein R_6 is C_1-C_4 alkyl.

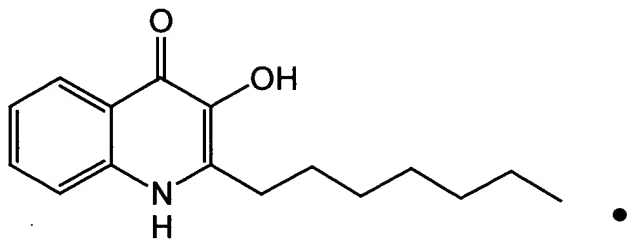
11. (Amended) The compound of claim [2]1, wherein R_5 is SH, O-R_6, or N-R_7R_8.

12. (Amended) The compound of claim [2]1, wherein X is O.

17. (Amended) The compound of claim [2]1, wherein the compound contains a chiral center.

18. (Amended) The compound of claim [2]1, which is an optically active isomer.

19. (Amended) The compound of claim 1, [comprising]having the formula II:

(II) 

20. (Amended) A compound of claim 1 or 19, wherein said compound is an autoinducer molecule [comprising a compounds of any one of claims 1, 2 or 19].

21. The compound[autoinducer molecule] of claim 20, [that]wherein said compound regulates gene expression.

22. The compound[autoinducer molecule] of claim 21, [that]wherein said compound regulates gene expression in bacteria.

23. The compound[autoinducer molecule] of claim 22, wherein said bacteria is *Pseudomonas aeruginosa.*

24. The compound[autoinducer molecule] of claim 23, wherein said gene expresses a virulence factor.

25. The compound[autoinducer molecule] of claim 24, wherein the virulence factor is elastase.

26. The compound[autoinducer] of claim 20, [that]wherein said compound regulates the activity of the LasR protein of *Pseudomonas aeruginosa.*

27. The compound[autoinducer] of claim 20, [that]wherein said compound regulates the activity of the RhlR protein of *Pseudomonas aeruginosa*.

28. The compound[autoinducer molecule] of claim 20, [that]wherein said compound is isolated from culture media in which *Pseudomonas aeruginosa* is grown.

29. A compound of claim[s] 1, [or 2 that]wherein said compound modulates the autoinducer activity of 2-heptyl-3-hydroxy-4-quinolone.

32. A compound of claim[s] 1, [or 2 that]wherein said compound modulates the activity of the LasR and/or the RhlR proteins of *Pseudomonas aeruginosa*.

34. (Amended) The compound of claim 32 that is an [antagonist]agonist of the LasR and/or the RhlR proteins of *Pseudomonas aeruginosa*.